NATIONAL MARROW DONOR PROGRAM®

BE THE MATCH®

October 30, 2013

LCDR Christopher Steele
Office of Naval Research
Code 34 – Warfighter Performance
875 N. Randolph St.
Arlington, VA 22203-1995

Subject: **Quarterly Performance/Technical Report of the National Marrow Donor Program®**

Reference: Grant Award #N00014-13-1-0039 between the Office of Naval Research and the National Marrow Donor Program

Dear LCDR. Steele:

Enclosed is subject document which provides the performance activity for each statement of work task item of the above reference for the period of July 1, 2012 to September 30, 2013.

Should you have any questions as to the scientific content of the tasks and the performance activity of this progress report, you may contact our Chief Medical Officer – Dennis L Confer, MD directly at 612-362-3425.

With this submittal of the quarterly progress report, the National Marrow Donor Program has satisfied the reporting requirements of the above reference for quarterly documentation. Other such quarterly documentation has been previously submitted under separate cover.

Please direct any questions pertaining to the cooperative agreement to my attention at 612-362-3403 or at cabler@nmdp.org.

Sincerely,

Carla Abler-Erickson

Carla Abler-Erickson, MA
Contracts Manager

Enclosure: Quarterly Report with SF298

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14. ABSTRACT

1. Contingency Prepardness: Collect information from transplant centers, build awareness of the Transplant Center Contingency Planning Committee and educate the transplant community about the critical importance of establishing a nationwide contingency response plan.

2. Rapid Identification of Matched Donors : Increase operational efficiencies that accelerate the search process and increase patient access are key to preparedness in a contingency event.

3. Immunogenetic Studies: Increase understanding of the immunologic factors important in HSC transplantation.

4. Clinical Research in Transplantation**:** Create a platform that facilitates multicenter collaboration and data management.

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Research in HLA Typing, Hematopoietic Stem Cell Transplantation and Clinical Studies to Improve Outcomes

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NATIONAL MARROW DONOR PROGRAM®

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Grant Award N00014-13-1-0039

DEVELOPMENT OF MEDICAL TECHNOLOGY FOR CONTINGENCY RESPONSE TO MARROW TOXIC AGENTS

QUARTERLY PERFORMANCE / TECHNICAL REPORT

FOR

JULY 01, 2013 to SEPTEMBER 30, 2013

PERIOD 3

Office of Naval Research

And

The National Marrow Donor Program
3001 Broadway Street N.E.
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QUARTER PROGRESS REPORT

Development of Medical Technology for Contingency Response to Marrow Toxic Agents

July 01, 2013 through September 30, 2013

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IIA. Contingency Preparedness – Objective 1: Recovery of casualties with significant myelosuppression following radiation or chemical exposure is optimal when care plans are designed and implemented by transplant physicians

IIA.1 Task 1: *Maintain the Radiation Injury Treatment Network (RITN) to prepare for the care of patients resulting from a hematopoietic toxic event.*

Period 3 Activity:

- Mayo Clinic conducted a RITN supported radiological disaster full scale exercise:
  - Phase I (8/23/13): Public Information Workshop Exercise: Initial notification and activation of NDMS. The workshop developed internal agency messaging and developed external community/media messaging.
  - Phase II (8/26/13): NDMS triage: Tested communication, pre-arrival triage/placement decision making (including patient family care planning, in collaboration with community partners), activated surge plans, and conducted patient transfers to regional clinics between Mayo Clinic and Hospital Disaster Preparedness & Response Compact members.
  - Phase III (8/27/13): Full-Scale - role-player/mannequin patients were triaged, radiological surveys conducted, patient decontamination evaluated but was unnecessary, and conducted patient movement. Continued Hospital Emergency Operations Center (HICS Coordination Center) coordination activities with internal departments and external partners.
  - Exercise observers included DHHS-ASPR & DHHS-BARDA staff, Dana-Farber Cancer Institute Staff (who will conduct the 2014 RITN Full Scale exercise in Boston) as well as RITN Control Team members.
- RITN Medical Advisor activity; Dr. Weinstock participated in the following activities supporting the Radiation Injury Treatment Network:
  - Was an invited speaker and member of the Organizing Committee for the CMCR/RITN Conference in Baltimore, MD in August 2013
  - Participated in the organization and editing of grant requests to BARDA for funding to support a G-CSF user managed inventory program through an interagency agreement with the Office of Naval Research.
  - Worked with representatives of the Department of Health and Human Services to pursue funding for a G-CSF user managed inventory program through the Hospital Preparedness Program

- Assisted with the 2013 RITN tabletop exercise
- Provided guidance to commercial entities (Cellerant, DxTerity, Sanofi) with interest in developing radiation countermeasures
- Assisted with the recruitment of new RITN centers
- Updated the RITN Grand Rounds Presentation to include guidance to centers that need to obtain HLA typing
- Co-authored the chapter on Nuclear and Radiological Events in KOENIG & SCHULTZ: Disaster Medicine, 2nd Edition

- Conducted a conference with the Centers for Medical Countermeasures against Radiation in Baltimore with 172 attendees. Activity is detailed in the 0142 quarterly report.
- Conducted three monthly RITN Center conference calls to review task completion status and allow a venue for centers to talk to peers.

IIA.1 Task 2: *GCSF in Radiation Exposure – This task is closed.*

IIA.1 Task 3: *Patient Assessment Guidelines and System Enhancements – This task is closed*

IIA 1 Task 4: *National Data Collection Model – This task is closed.*

IIA. Contingency Preparedness – Objective 2: Coordination of the care of casualties who will require hematopoietic support will be essential in a contingency situation.

IIA.2 Task 1: *Ensure NMDP maintains effective plans to continue critical facility and staff-related functions as a result of operations interruption events.*

Period 3 Activity:

- Conducted user testing of the Governmental Emergency Telecommunications Service (GETS).
- Continued to coordinate an exercise to test the ability of the Repository to move the KitMaker operations in the event that the Repository building is not habitable.

IIA.2 Task 2: *Sibling Typing Standard Operating Procedures – This task is closed*

IIA. Contingency Preparedness – Objective 3: NMDP's critical information technology infrastructure must remain operational during contingency situations that directly affect the Coordinating Center.

IIA.3 Task 1: *I.S. Disaster Recovery – This task is closed.*

IIA.3 Task 2: *Critical Facility and Staff Related Functions – This task is closed.*

IIB. Rapid Identification of Matched Donors – Objective 1: Increasing the resolution and quality of the HLA testing of volunteers on the registry will speed donor selection.

IIB.1 Task 1: *Expand the genetic diversity of the Registry through continued addition of adult donors and cord blood units, utilizing high volume HLA typing methodologies.*

Period 3 Activity:

2-Step Activation at Live Drive Registration:

- The 2-Step Activation Phase Two Pilot launched on March 28, 2013. Phase Two includes an online activation channel, in addition to the Phase One channels of phone and text activation.
- The pilot period was extended for one additional month to August . In Phase Two, 4051 individuals participated in live drive registration through the 2-Step Activation process. Analysis of the determinants of activation/non-activation is underway.

HLA Mischaracterization Research

Alleles that are less common in the Be The Match Registry were evaluated to determine whether results may have been incorrectly reported based on rules established in previous typing projects. These rules include:

- Alleles reported prior to 2004
- Reported in a subject whose self described race is different than what was reported for the allele in the IMGT/HLA database

- Uncommon alleles reported with another uncommon/rare allele
- Alleles reported consistently with the same second allele.

During this quarter, 118 samples were typed for intermediate HLA-A, B, or C and 188 samples were typed at intermediate resolution DRB1. Samples previously typed at intermediate resolution, where the suspicious allele was confirmed, were then requested for high resolution sequence based typing (SBT) to verify the intermediate resolution typing methodology correctly resolved the allele. SBT was completed on 18 samples for HLA-A, 10 samples for HLA-B, 12 for HLA-C, and 8 HLA-DRB1. The SBT confirmed the intermediate resolution reporting in all samples but one. The one incorrectly reported allele indicates an error in the specificity of the reagents utilized and this information will be used to identify others samples with this same interpretation issue.

IIB.1 Task 2: *Evaluate HLA-DRB1 High Res typing – This task is closed.*

IIB.1 Task 3: *Evaluate HLA-C Typing of Donors – This task is closed*

IIB.1 Task 4: *Evaluate the suitability of buccal swabs as a method to collect DNA samples to HLA type casualties and potential related donors in contingency situations, and to obtain research samples.*

Period 3 Activity:

Alternate Sample Collection Methods:

- **Biospecimen Physical Preservation.** A Consultant completed an analysis report this quarter. The report addressed the feasibility of simple treatments to enhance the DNA stabilization of buccal swab samples stored in room temperature or frozen conditions. Current commercial and academic research approaches were evaluated. The report is under review, to determine next steps.

IIB 1 Task 5: *Evaluate the factors of donor utilization and speed of search process after strategic upgrading of selected adult volunteer donors.*

Period 3 Activity:

- No activity this period.

IIB 1 Task 6: *Maintain a comprehensive quality control program.*

Period 3 Activity:

- No activity this period.

IIB. Rapid Identification of Matched Donors – Objective 2: Primary DNA typing data can be used within the registry to improve the quality and resolution of volunteer donor HLA assignments.

IIB 2 Task 1: *Ongoing collection of primary data for validation and storage in the Registry database.*

Period 3 Activity:

- Gathered requirements and initiated development of HML 1.0 specification to address community feedback on the current formats and incorporate new constructs for Next-Generation Sequencing.

IIB 2 Task 2: *Validation of Logic of Primary Data – This task is closed.*

IIB 2 Task 3: *Reinterpretation of Primary Data – This Task has been merged with Task IIB2.4.*

IIB 2 Task 4: *Interpretation of the primary data into genotype lists and integration into matching algorithm to optimize placement of donors onto patient searches.*

Period 3 Activity:

- HL7:
    - Attended HL7 Working Group Meeting in Cambridge MA, Sep 23-27; met with working groups for Clinical Genomics, Structured Documents, and Orders & Observations.
    - Presented constrained CDA for HLA typing to Clinical Genetics Work Group.
    - Participated in weekly Clinical Genomics Workgroup meetings.
- Deployed new versions of the Silver Standard genotype list storage RESTful web service to gl.immunogenomics.org
- Continued development using an entropy calculation on typing frequencies to compute a Typing Ambiguity Score

- Continued developing databases for IMGT allele tool for the public.
- IMMPUTE project – to validate algorithms to impute HLA typings from MHC region SNP data
    - Conducted more evaluation experiments on imputation results submitted by IMMPUTE participants. Measured:
        - Overall accuracy per locus
        - Population-specific accuracy per locus
        - Compared the methods based on their accuracy per locus, and with respect to different prediction likelihood thresholds
    - Compared the methods based on accuracy in different allele groups for every HLA locus

IIB. Rapid Identification of Matched Donors – Objective 3: Registry data on HLA allele and haplotype frequencies and on the nuances of HLA typing can be used to design computer algorithms to predict the best matched donor.

IIB.3 Task 1: *Incorporate HLA allele and haplotype frequencies into matching algorithm.*

Period 3 Activity:

- Implemented changes to the matching algorithm, based on approval from Histocompatibility Advisory Group, to make antigen match grade assignments based on probabilities. This paves the way for the removal of allele codes from the matching equation and the constraints on the allele code system to not allow certain allele combinations.

IIB 3 Task 2: *Continue to enhance the allele and haplotype frequency data to include additional loci and increased resolution for ethnic groups with input from consultants with expertise in population genetics.*

Period 3 Activity:

- The goal of this task is to validate allele predictions for various minority populations using NMDP registry donors. A total of 648 donors of Hispanic ethnicity were sent to a contract lab for 6 locus (A-B-C-DRB1-DQB1-DPB1) high resolution typing. These donors were previously identified as unspecified Hispanic. After participating in an ancestry questionnaire, where they were instructed to select a country of origin and give parental background information, their populations were specifically defined. High resolution typing results from 70% of these donors at all 6 loci of interest were received by the

end of this quarter. Each donor's haplotype as predicted by the HapLogic III Haplostats tool will be compared to the actual typing of the donor as reported by the contract lab. The alleles will be predicted based off the original recruitment typing and the population the donor identified as on the ancestry questionnaire. By comparing the Haplostats prediction to the actual typing, we will be able to detect potential inconsistencies or variation in the Hispanic sub-populations of the Caribbean islands and Mexico.

- Calculated genomic-level 6-locus haplotype frequencies.
- Calculated 6-locus population frequencies for Caucasian subpopulations.
- Calculated 9-locus US haplotype frequencies including DQA1, DPA1, DPB1 loci.
- Calculated typing ambiguity score on all subjects used to generate haplotype frequencies – may be used as a threshold to exclude highly ambiguous typings.
- Made improvements to the EM (Expectation Maximization) analysis Pipeline (to improve re-computing Haplotype frequencies that are used in matching), we have reduced run time of one of the modules significantly.

IIB 3 Task 3: *Cord Blood and Adult Donor Matching Benchmarks and Registry Modeling.*

Period 3 Activity:

- More modeling has been carried out for NIMA to show improved match rates.
- A poster was developed describing the impact of NIMA match modeling on CBU selection and availability for presentation at the Fall WMDA meeting.

IIB 3 Task 4: *Couple haplotype prediction methodology with donor demographic data to target recruitment to areas populated by individuals with underrepresented HLA phenotypes.*

Period 3 Activity:

- Developing ongoing additional improvements to Copula imputation to eliminate remaining no calls using synthetic haplotype frequencies.
- The manuscript titled "Validation of Statistical Imputation of Allele-Level Multi-Locus Phased Genotypes from Ambiguous HLA Assignments" has been submitted to the journal Tissue Antigens.

- Validation of amino acid imputation of simulated serological typings of individuals has been completed.
- Ancestry Questionnaire Pilot
    - Pilot questionnaire has been mailed to all donors selected for participation in the pilot cohort
    - First round of SNP genotyping was completed and data received
    - First round of analysis was completed, showing that the pilot questionnaire demonstrated an enhanced capability to capture and race and ethnic information on MULTI and HIS donors that correlate with genetically inferred information via ancestry informative markers and HLA.
- EM validation
    - Developed a framework for validation of haplotype frequencies generated by EM. The framework was tested on simulated data as well as the registry haplotype frequencies generated by different versions of EM algorithm.
- Typing ambiguity score and HaploStats
    - Designed a measure to evaluate ambiguity contained in HLA typing, which takes into account the number of possible non-ambiguous typings as well as the distribution of their likelihoods. The measure, termed typing ambiguity score, ranges from zero to one, one being non-ambiguous typing. The typing ambiguity score was applied to a number of simulated datasets, describing HR, SBT, SSO and serological typing methodologies, in order to quantify the average ambiguity being produced by each methodology.
    - Worked to integrate the typing ambiguity score into the pipeline for evaluating historic registry typing.
    - Worked on integrating typing ambiguity score into HaploStats, a web-tool that provides HLA imputation and summary of ambiguous HLA data using population haplotype frequencies.

Disease association methods development

- Provided statistical analysis for a Multiple Myeloma disease association project, including development of a more reliable method to correct for family wise error rates. False Discovery Rate was implemented to check for significance after adjustment at each loci/haplotype.
- Completed implementation of a factor analysis on allele and haplotype groups as well as single amino acid polymorphisms and sequence feature variant types (SFVT) to incorporate HLA linkage disequilibrium into our statistical model for disease

association studies.

IIB 3 Task 5: *Develop a bioinformatics web site for frequency information.*

Period 3 Activity:

- Initiated migration of content to the new site. Content migration is focused on the bioinformatics tools, haplotype frequencies, data standards, publications, and social media.
- Multimedia production for “HLA: Making the Match" video, completed the last half of the video which included:
  - Revised the script
  - Re-recorded and edited narration
  - Revised several illustrations and animations
  - Formatted video for display on the web site

IIB 3 Task 6: *Use NMDP’s expert Search Strategy Advisors as resources to further improve the matching algorithm and donor/cord blood identification software applications with the goal to maximize the ability of the software to identify the best donors/cords for each patient.*

Period 3 Activity:

- Primary software development for the implementation of a search archive was completed.

IIB 3 Task 7: *Population Genetics – This task was merged with Task IIB3.2*

IIB 3 Task 8: *Haplotype Matching – This task was merged with Task IIB3.2*

IIB 3 Task 9: *Global Haplotype/Benchmark – This task was merged with Task IIB3.3*

IIB. Rapid Identification of Matched Donors – Objective 4: Reducing the time and effort required to identify closely matched donors for patients in urgent need of HSC transplants will improve access to transplantation and patient survival in the context of a contingency response and routine patient care.

IIB.4 Task 1: *Expand Network Communications – This task is closed.*

IIB.4 Task 2: *Conduct a study of random patient search simulations to test the efficacy of centralized contingency management.*

Period 3 Activity:

- NMDP provided support for donor/cord blood unit identification, selection and collection for the NIH intramural unrelated donor transplant program. Activity in the last quarter was as follows:
    - 4 PBSC collections
- CIBMTR provided support for the rapid identification of potential donors for newly diagnosed AML patients under the following clinical trial protocol:
    - S1203: A Randomized Phase III Study of Standard Cytarabine plus Daunorubicin (7+3) Therapy or Idarubicin with High Dose Cytarabine (IA) versus IA with Vorinostat (IA+V) in Younger Patients with Previously Untreated Acute Myeloid Leukemia (AML)
    - CIBMTR provided study-specific sample collection kits for patients, processed samples, arranged HLA typing, and generated preliminary search strategy reports to assist in the identification of donors and/or CBU through the NMDP.
    - It is anticipated that 750 patients will be accrued in less than 5 years with 40% needing HLA testing and search strategy results. The trial opened in April 2013. Activity during the quarter:
        - 51 patients enrolled and 54 sample collection kits distributed
        - 10 patients identified as high risk
            - 12 HLA typed and preliminary search reports completed

IIB.4 Task 3: *Benchmarking Analysis – This task is closed*

IIB.4 Task 4: *Expand Capabilities of Collection and Apheresis Centers – This task is closed.*

IIC. Immunogenetic Studies – Objective 1: HLA mismatches may differ in their impact on transplant outcome, therefore, it is important to identify and quantify the influence of specific HLA mismatches. In contingency situations it will not be possible to delay transplant until a perfectly matched donor can be found.

IIC.1 Task 1: *Continue to evaluate HLA disparity and impact on HSC transplantation by adding selected pairs to the Donor/Recipient Pair project utilizing sample selection criteria that optimize the new data generated by the typing project.*

Period 3 Activity:

Donor Recipient Pair Project

In 1994 a retrospective D/R Pair HLA typing project to characterize class I and class II alleles of donor/recipient paired samples from NMDP's Repository was initiated. The goals of this ongoing research project are to assay the impact of DNA-based HLA matching on unrelated donor transplant outcome, develop strategies for optimal HLA matching, evaluate the impact of matching at alternative HLA loci on transplant outcome and finally to promote the development of DNA-based high resolution HLA typing methodologies. Presence/absence typing of 16 Killer Immunoglobulin-Like Receptor (KIR) loci (2DL1-5, 2DS1-5, 3DL1-3, 3DS1, 2DP1 and 3DP1) has been included.

- Auditing of SG30 KIR and SG31 HLA and KIR continued.
- Analysis of an RFQ that went out to the participating laboratories on April 22, 2013 with responses received on May 6, 2013, was completed this quarter. Future SG contracts will be awarded based on this analysis.
- SG 32 consisting of 402 single cord blood transplants, 299 double cord blood transplants and 843 donor/recipient transplants was contracted September 1, 2013. The period of performance came to a close on September 30, 2013.
- Pseudo gene (KIR*2DP1 and KIR*3DP1) typing data not initially reported with previous KIR typings is still being collected from all of the laboratories.

Most clinical association studies of KIR have analyzed at presence/absence resolution for each gene. Although the region has long been known to be both allelically and structurally diverse, the extent of copy number variation (CNV) has only started to be clarified. CNV data has the potential to improve, association studies by reducing confounding factors and increasing haplotypic resolution.

- Analysis of the full KIR genotyped samples with CNV assignments is ongoing.
    - Future CNV typing will include all haplotype variants as well as all minority samples previously genotyped.

Current HLA matching guidelines for unrelated HCT recommend avoidance of mismatches within the Antigen Binding Domain (ABD). This recommendation is based on the hypothesis that amino acid differences outside the ABD are not immunogenic. The ABD allo-reactivity assessment project aims to provide insight impact of mismatching outside of the ABD.

- The results of the class I and II analyses were summarized in two abstracts submitted to the 2013 ASHI meeting. The class I and class II analyses were accepted for poster and oral presentation, respectively.
- Queries of DRB1*14:01:01/14:54 haplotypes identified additional registry member that could be included in the study.
- Analysis of the potential donors HLA typing has provided four haplotype pair cohorts that will be further typed.
- A total of 334 high resolution typing panels at A, B, C, DRB1/3/4/5, DQB1 and DPB1 will be performed to allow selection for future donor contact.

IIC. Immunogenetic Studies – Objective 2: Even when patient and donor are HLA matched, GVHD occurs so other loci may play a role.

IIC.2 Task 1: *Continue to develop typing protocols for non-HLA immunogenetic loci, development of a lab network, enhancement of database to capture non-HLA data and continue analyses to evaluate genetic diversity in the transplant population.*

Period 3 Activity:

- Immunobiology Integration Data Base (IIDB)
    - Implemented an HLA Validation Service that applies NMDP Operational rules for the validation of non-NMDP facilitated data (e.g. CIBMTR forms)
    - Added non-NMDP-facilitated HLA typing information to the CIBMTR data warehouse and computed match grades using the NMDP HapLogic III algorithm.
- Clinical Ancestry Study
    - Pilot analysis has been complete, two analyses have been performed:
        - Effect of donor/recipient genetic disparity on transplant outcome: Multivariate analysis on seven outcomes

suggests there are trends worth investigating further. However, most p-values were not significant as the number of donor/recipient pairs in the discovery pilot was small.

- Effect of recipient admixture on transplant outcome. Four main recipient admixtures were analyzed for all recipients in the pilot cohort: EUR, AFR, NAM and ASI. Again there were trends which require a larger sample to show statistical significance.

- A power analysis was conducted for a second larger phase of the study that is currently being planned.

IIC 2 Task 2: *Related Pairs Research Repository – This task is closed.*

IIC 2 Task 3: *CIBMTR Integration – This task is closed.*

IID. Clinical Research in Transplantation – Objective 1: Clinical research in transplantation improves transplant outcomes and supports preparedness for a contingency response.

IID.1 Task 1: *Conduct observational research and interventional clinical trials.*

Period 3 Activity:

Observational Research

- The observational research program supported the submission of 25 abstracts to the ASH 2013 annual meeting. Seventeen abstracts were accepted for oral and 8 for poster presentation. This represents the most abstracts ever submitted to ASH by the CIBMTR in a single year.

Prospective Studies; RCI BMT

- Staff worked during this reporting period on final dataset preparation for the 05-DCB (Adult Double Cord) trial. A final draft of the manuscript is completed and study team review in process prior to submission for publication.
- Survey Research Group (SRG) staff continued to perform outreach to accrued donors on the long-term donor follow up study whose follow-up time point became due during the quarter. A total of 1,432 donors were contacted and forms completed. Donor Centers continue to actively perform consent sessions with donors during their standard work-up process. During this reporting period overall accrual reached just over 16,000 donors, ~49% of the accrual goal of 32,128.

- Staff worked on improvements to the long term donor follow-up trial reports and data cleaning of the reported event confirmation data.
- Work continued on logistical plans to provide non-NMDP operated donor centers with donor follow up activities through the SRG. This will further standardize the processes and is expected to increase the overall completed time points. It is anticipated that any interested donor center would transition at the time of the donor module release in the FormsNet3 application.
- Staff from the RCI BMT continued to work with CIT staff to explore options for a) comprehensive system for management of activities and studies within the SRG and b) clinical trial management system (CTMS) to coordinate operational and administrative activities within RCI BMT. The CIT technical team continued to refine design options following the design review process.
- Logistics planning continued on the new donor research sample project, Astellas. Donor center training which meets the company's requirements is being finalized. It is anticipated the project will be initiated during period 5 of this contract.

Cord Blood Research Subcommittee

The assessment of testing variability was completed for the post validation phase of the study investigating biomarkers associated with cord blood engraftment.

- The study group decided to halt the study based on the poor reliability results and lack of continuing interest in developing the assay from the validation laboratory.

Work continued on the development of the anti-HLA donor specific antibody study of recipients transplanted with CBUs.

- Cohort and graft failure cases were identified.
- Next steps include protocol finalization and laboratory contracting.

Work continued on a study to assess CBU characteristics (viability, TNC, CFU and CD34) pre-freeze and post thaw.

- The study protocol and data collection forms were finalized.
- The study population was finalized and will include 944 cases of single CBU transplants.

- Participation agreements were finalized with the study cord blood banks and lists of cases distributed for data capture.
- Data submission will be completed next quarter.

IID.1 Task 2: *Research with NMDP Donors – This task was merged with IID1.1.*

IID.1 Task 3:

Expand support for immunobiology research, statistical genetics and clinical research studies under CIBMTR Immunobiology Working Committee.

Period 3 Activity:

The CIBMTR IBWC met monthly during the quarter to discuss progress on ongoing research studies.

- Six abstracts were submitted and accepted:
  - Sarah Cooley, et al., *Recipient HLA-C1 enhances the clinical advantage of killer-cell immunoglobulin-like receptor B haplotype donors in myeloablative unrelated transplantation for acute Myelogenous leukemia.* ASH 2013 annual meeting, accepted for oral presentation.
  - John Koreth, et al., *HLA-mismatch is associated with worse outcomes after unrelated donor reduced intensity conditioning hematopoietic cell transplantation: A CIBMTR Analysis.* ASH 2013 annual meeting, accepted for oral presentation.
  - Salyka Sengsayadeth, et al., *Cytotoxic T lymphocyte antigen 4 (CTLA4) single nucleotide polymorphisms do not impact outcomes after unrelated donor transplant: A CIBMTR Analysis.* ASH 2013 annual meeting, accepted for oral presentation.
  - Michelle Gleason, et al., *A novel CD16xCD33 bispecific killer cell engager (BiKE) mediates a double hit for natural killer (NK) cells to target DC33+ myelodysplastic syndrome (MDS) cells and myeloid derived suppressor cells (MDSC) at all disease stages.* ASH 2013 annual meeting, accepted for oral presentation.
  - Ronald Sobecks, et al., *Influence of killer immunoglobulin-like receptor (KIR) and HLA genotypes on outcomes after refuced-intensity conditioning allogeneic hematopoietic stem cell transplantation for patients with AML and MDS: A report from the CIBMTR Immunobiology Working Committee.* ASH 2013 annual meeting, accepted for oral presentation.
  - Payal Khincha, et al., *Evaluating the utility of telomere length measurement by qPCR as a diagnostic test for*

dyskeratosis congenital. ASH 2013 annual meeting, accepted for poster presentation.

- Three manuscripts were submitted:
  - Mary Eapen, et al., *Impact of allele-level HLA matching on outcomes after myeloablative single unit umbilical cord blood transplantation for hematologic malignancy.* Submitted to Blood.
  - Katharina Fleischhauer, et al., *Risk-associations between HLA-DPB1 T cell epitope matching and outcome of unrelated hematopoietic cell transplantation are independent from HLA-DPA1.* Submitted to Blood
  - Effie Petersdorf, et al., *HLA-C expression levels define permissible mismatches in hematopoietic cell transplantation.* Submitted to Nature Medicine.
- Four manuscripts were published:
  - Joseph Pidala, et al., *Amino acid substitution at peptide-binding pockets of HLA class I molecules increases risk of severe acute GVHD and mortality.* Blood, Aug. 27, 2013, Epub ahead of print
  - Zaiba Shamim, et al., *Polymorphism in the interleukin-7 receptor-alpha and outcome after allogeneic hematopoietic cell transplantation with matched unrelated donor.* Scand J Immunol. 2013 Aug;78(2):214-20.
  - Yasuo Morishima, et al., *Significance of ethnicity in the risk of acute graft-versus-host disease and leukemia relapse after unrelated donor hematopoietic stem cell transplantation.* Biol Blood Marrow Transplant. 2013 Aug;19(8):1197-203.
  - Noriko Isobe, et al., *Genetic risk variants in African Americans with multiple sclerosis.* Neurology. 2013 Jul 16;81(3):219-27.

ACRONYM LIST

AABB	American Association of Blood Banks	HML	Histoimmunogenetics Mark-up Language
AFA	African American	HR	High Resolution
AFR	African American	HRSA	Health Resources and Services Administration
AGNIS	A Growable Network Information System	HSC	Hematopoietic Stem Cell
ABD	Antigen Binding Domain	IBWC	Immunobiology Working Committee
AML	Acute Myelogenous Leukemia	ICRHER	International Consortium for Research on Health Effects of Radiation
API	Asian Pacific Islander	IIDB	Immunobiology Integration Data Base
AQP	Ancestry Questionnaire Project	IDM	Infectious Disease Markers
ARS	Acute Radiation Syndrome (also known as Acute Radiation Sickness)	IHWG	International Histocompatibility Working Group
ASBMT	American Society for Blood and Marrow Transplantation	IMGT	International ImMunoGeneTics
ASHI	American Society for Histocompatibility and Immunogenetics	IPR	Immunobiology Project Results
ASI	Asian	IND	Investigational New Drug
ASTHO	Association of State and Territorial Health Officials	IS	Information Services
B-LCLs	B-Lymphoblastoid Cell Lines	IT	Information Technology
BARDA	Biomedical Advanced Research and Development Authority	IRB	Institutional Review Board
BBMT	Biology of Blood and Marrow Transplant	JCAHO	Joint Commission on Accreditation of Healthcare Organizations
BCP	Business Continuity Plan	KIR	Killer Immunoglobulin-like Receptor
BCPeX	Business Continuity Plan Exercise	MDACC	MD Anderson Cancer Center
BMCC	Bone Marrow Coordinating Center	MDS	Myelodysplastic Syndrome
BMDW	Bone Marrow Donors Worldwide	MHC	Major Histocompatibility Complex
BMT	Bone Marrow Transplantation	MICA	MHC Class I-Like Molecule, Chain A
BMT CTN	Blood and Marrow Transplant - Clinical Trials Network	MICB	MHC Class I-Like Molecule, Chain B

BODI	Business Objects Data Integrator	MKE	Milwaukee
BRT	Basic Radiation Training	MRD	Minimal Residual Disease
C&A	Certification and Accreditation	MSKCC	Memorial Sloan-Kettering Cancer Center
CAU	Caucasian	MSP	Minneapolis
		MUD	Matched Unrelated Donor
CBMTG	Canadian Blood and Marrow Transplant Group	MULTI	Multiple
CBB	Cord Blood Bank	NAC	Nuclear Accident Committee
CBC	Congressional Black Caucus	NACCHO	National Association of County & City Health Officials
CBS	Canadian Blood Service	NAM	Native American
CBU	Cord Blood Unit	NARR	National Alliance for Radiation Readiness
CD	Cell Differentiation	NCBI	National Center for Biotechnology Information
CDA	Clinical Document Architecture	NCBM	National Conference of Black Mayors
CFU	Colony Forming Unit	NCI	National Cancer Institute
CHORI	Children's Hospital of Oakland Research Institute	NDMS	National Disaster Medical System
CHTC	Certified Hematopoeitic Transplant Coordinator	NEMO	N-locus Expectation-Maximization using Oligonucleotide typing data
CIBMTR®	Center for International Blood & Marrow Transplant Research	NGS	Next Generation Sequencing
CIT	CIBMTR Information Technology	NHLBI	National Heart Lung and Blood Institute
CLIA	Clinical Laboratory Improvement Amendment	NIH	National Institutes of Health
CMCR	Centers for Medical Countermeasures Against Radiation	NIMA	Non-Inherited Maternal Antigen
CME	Continuing Medical Education	NIMS	National Incident Management System
CMF	Community Matching Funds	NK	Natural Killer
CMV	Cytomegalovirus	NLE	National Level Exercise
CNV	Copy Number Variation	NMDP®	National Marrow Donor Program
COG	Children's Oncology Group	NRP	National Response Plan
CREG	Cross Reactive Groups	NST	Non-myeloablative Allogeneic Stem Cell Transplantation

CSS	Center Support Services	OCR/ICR	Optical Character Recognition/Intelligent Character Recognition
CT	Confirmatory Testing	OIT	Office of Information Technology
CTA	Clinical Trial Application	OMB	Office of Management and Budget
CTMS	Clinical Trial Management System		
DC	Donor Center	ONR	Office of Naval Research
DCB	Double Cord Blood		
DHHS-ASPR	Department of Health and Human Service – Assistant Secretary Preparedness and Response	P2P	Peer-to-Peer
DIY	Do it yourself	PBMC	Peripheral Blood Mononuclear Cells
DKMS	Deutsche Knochenmarkspenderdatei	PBSC	Peripheral Blood Stem Cell
DMSO	Dimethylsulphoxide	PCR	Polymerase Chain Reaction
DoD	Department of Defense	PSA	Public Service Announcement
DNA	Deoxyribonucleic Acid	QC	Quality control
DR	Disaster Recovery	RCC	Renal Cell Carcinoma
D/R	Donor/Recipient	RCI BMT	Resource for Clinical Investigations in Blood and Marrow Transplantation
DSTU	Draft Standard for Trial Use	REAC/TS	Radiation Emergency Assistance Center/Training Site
EBMT	European Group for Blood and Marrow Transplantation	REST	Representational State Transfer
ED	Emergency Department	RFP	Request for Proposal
EDC	Electronic Data Capture	RFQ	Request for Quotation
EFI	European Federation of Immunogenetics	RG	Recruitment Group
EM	Expectation Maximization	RITN	Radiation Injury Treatment Network
EMDIS	European Marrow Donor Information System	SBT	Sequence Based Typing
ENS	Emergency Notification System	SCTOD	Stem Cell Therapeutics Outcome Database
ERSI	Environment Remote Sensing Institute	SG	Sample Group
EUR	European	SHF	Synthetic Haplotype Frequency
FBI	Federal Bureau of Investigation	SLCBB	St. Louis Cord Blood Bank
FDA	Food and Drug Administration	SLW	STAR Link® Web
FDR	Fund Drive Request	SSA	Search Strategy Advice

FLOCK	Flow Cytometry Analysis Component	SSO	Sequence Specific Oligonucleotides
Fst	Fixation Index	SSP	Sequence Specific Primers
GETS	Government Emergency Telecommunications Service	SSOP	Sequence Specific Oligonucleotide Probes
GCSF	Granulocyte-Colony Stimulating Factor (also known as filgrastim)	STAR®	Search, Tracking and Registry
GIS	Geographic Information System	TC	Transplant Center
GS	General Services	TED	Transplant Essential Data
GTR	Genetic Testing Registry	TNC	Total Nucleated Cell
GvHD	Graft vs Host Disease	TSA	Transportation Security Agency
HCS®	HealthCare Standard	UCSF	University of California – San Francisco
HCT	Hematopoietic Cell Transplantation	UI	User Interface
HEPP	Hospital Emergency Preparedness Program	UML	Unified Modeling Language
HHQ	Health History Questionnaire	URD	Unrelated Donor
HHS	Health and Human Services	WGA	Whole Genome Amplification
HIPAA	Health Insurance Portability and Accountability Act	WMDA	World Marrow Donor Association
HIS	Hispanic	WU	Work-up
HLA	Human Leukocyte Antigen		